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(71) Applicants and

(72) Inventors: **GARDELLA, Thomas, J.** [US/US]; 1045
Greendale Avenue, Needham, MA 02492 (US). **KRO-**
NENBERG, Henry, M. [US/US]; 50 Blossom Street,
Boston, MA 02114 (US). **POTTS, John, T.** [US/US];
Building 149, 13th Street, Charlestown, MA 02129-2000
(US).

(74) Agents: **BUGAISKY, Lawrence, B.** et al.; Sterne,
Kessler, Goldstein & Fox P.L.L.C., Suite 600, 1100 New
York Avenue, N.W., Washington, DC 20005-3934 (US).

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(54) Title: CONFORMATIONALLY CONSTRAINED PARATHYROID HORMONE (PTH) ANALOGS WITH LACTAM BRIDGES

(57) Abstract: The present invention relates to methods of treatment of mammalian conditions characterized by decreases in bone mass with conformationally constrained parathyroid hormone (PTH) analogs and derivatives of those analogs containing PTH polypeptide derivatives containing at least one Glu or Lys substitution at position 6 and/or 10, some with installed lactam bridges between the side chains of Lys and Glu. The invention provides derivatives of PTH (1-34), PTH(1-33), PTH(1-32), PTH(1-31), PTH(1-30), PTH(1-29), PTH(1-28), PTH(1-27), PTH(1-26), PTH(1-25), PTH(1-24), PTH(1-23), PTH(1-22), PTH(1-21), PTH(1-20), PTH(1-19), PTH(1-18), PTH(1-17), PTH(1-16), PTH(1-15), PTH(1-14), PTH(1-13), PTH(1-12), PTH(1-11), PTH(1-10) and PTH(1-9) polypeptide. The invention also provides methods of preparing the PTH analogs. Further, the invention encompasses treating conditions that are characterized by undesired bone loss or by the need for bone growth, e.g. in treating fractures or cartilage disorders and for raising cAMP levels in cells where deemed necessary.

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